REMARKS

Claims 1, 7-9, 40, and 42-64 are pending. Applicants have amended claims 8, 9, and 47 to clarify the invention. Support for this amendment can be found in the specification at, *inter alia*, page 7, lines 25-26 and page 8, lines 13-18. No new matter has been introduced, and Applicants respectfully request that the amendments and remarks made herein be entered into the record of the instant application. Claims 43-49 and 58-60 are allowed.

THE CLAIM REJECTIONS UNDER 35 U.S.C. § 102(b) SHOULD BE WITHDRAWN

Claims 1, 7-9, 40, 42, 50-57, and 61-64 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Bizik *et al.* (Int J Cancer. 1986 Jan 15;37(1):81-8, "Bizik"). Specifically, the Examiner alleges that the ammonium sulfate precipitation procedure described in Bizik on pages 81-82 results in the purified complexes or purified population of complexes of the instant invention. For the following reasons, Applicants respectfully disagree.

The legal standard for anticipation under 35 U.S.C. § 102 (b) is one of strict identity. In order to anticipate the claimed invention, a single reference must teach each and every element of the claims. *Verdegaal Bros. v. Union Oil Co.*, 814 F.2d 628, 2 U.S.P.Q.2d 1051 (Fed. Cir. 1987). In order to establish inherency, "the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *In re Robertson*, 169 F.3d 743 (Fed. Cir. 1999)(quoting *Continental Can Co. v. Monsanto Co.*, 948, F.2d 1264, 1268, (Fed. Cir. 1991)(internal quotations omitted). Inherency "may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *Id.* (quoting *Continental Can* at 1749).

Independent claims 1 and 7 relate to a purified molecular complex comprising an α2M polypeptide (which can be α2M or a subsequence thereof) comprising the α2M receptor binding domain noncovalently associated with an antigenic molecule. Independent claims 8 and 9 relate to a purified population of molecular complexes which are noncovalent complexes of (i) an α2M, and (ii) an antigenic molecule. Thus, all of the rejected independent claims specify a purified noncovalent complex(es) of α2M (or an α2M polypeptide) and an antigenic molecule. Applicants submit that Bizik does not expressly or inherently teach purified complexes of α2M noncovalently associated with an antigenic molecule, as specified in the claims of the instant application.

Bizik teaches that α2M was purified from conditioned media of a cancer cell line using a series of steps including ammonium sulfate precipitation followed by size-exclusion chromatography and finally preparative SDS-polyacrylamide gel electrophoresis ("SDS PAGE") followed by electroelution from the relevant gel slice (termed hereinafter, "the First Bizik Procedure") (see Bizik *et al.*, paragraph spanning pages 81 and 82; and Figure 1 on page 82). The Examiner's attention is directed to the Declaration of Dr. Kenneth Parker under 37 C.F.R. §1.32 submitted herewith. In paragraphs 9-11 of his Declaration under Rule 132, Dr. Kenneth Parker has presented evidence and reasoning in support of his conclusion that neither the ammonium sulfate precipitation step, nor the combination of ammonium sulfate precipitation with size exclusion chromatography of the First Bizik Procedure provides the purified complexes or purified population of complexes of the instant claims. Dr. Parker explains that "one skilled in the art typically construes the term 'purified protein' to mean a protein that has been separated substantially from other proteins, where 'separated substantially' in this context means such that, at a minimum, the protein of interest is the predominant protein by weight in the preparation" (see the Declaration of Dr. Parker at para. 11). Dr. Parker also notes that this meaning of "purified" is consistent with the usage of the term "purified" in the instant specification (see the Declaration of Dr. Parker at para. 11). Based on this standard definition of "purified protein", Dr. Parker concludes that neither the ammonium sulfate precipitation step nor the size exclusion chromatography step of Bizik produce the purified complexes or purified population of complexes of the instant invention because α2M is a minor component among the proteins present in the protein preparation produced by either step (see the Declaration of Dr. Parker at para. 11). In support of this finding, Dr. Parker refers to Bizik's SDS-PAGE analysis of the preparation obtained after the ammonium sulfate precipitation step, which shows that α2M is not even visible, let alone a minor component among the proteins present in the preparation (See Bizik, lane 1 of Figure 1 on page 82; the Declaration of Dr. Parker at para. 11). It is further noted by Dr. Parker that Bizik expressly states that bovine albumin was the most abundant component of the ammonium sulfate-precipitated proteins (see Bizik, page 83, col. 2; the Declaration of Dr. Parker at para. 11). Dr. Parker also refers to the SDS-PAGE analysis of the preparation obtained after the size exclusion chromatography step, which shows that α2M is clearly not the predominant protein by weight in the preparation (See Bizik, lane 2 of Figure 1 on page 82; the Declaration of Dr. Parker at para. 11). Dr. Parker characterizes the preparation obtained after the size exclusion chromatography step to be possibly " 'enriched for' α2M,

but not a purified α2M, in view of the standard meaning of the term 'purified'." (see the Declaration of Dr. Parker at para. 11). Thus, in view of the above and in light of Dr. Parker's Declaration under Rule 132, one of skill in the art would conclude that neither the ammonium sulfate precipitation step nor the size exclusion chromatography step taught in Bizik resulted in purified α2M-peptide complexes because α2M was a minor component among the proteins present in the protein preparation produced by either step.

Indeed, consistent with the foregoing, Bizik teaches only the α2M eluted from the preparative SDS-polyacrylamide gel slice as containing purified α2M since SDS-PAGE analysis following this step shows that α2M is the predominant protein by weight and there is no visible contamination by other proteins (see Bizik, lane 3 of Figure 1 on page 82; page 83, col. 2, ¶¶ 1 to page 84, col. 2l; the Declaration of Dr. Parker at para. 11). However, as discussed in the Amendment filed on August 14, 2006 (incorporated by reference herein), this purified α2M is not complexed to antigenic molecules. Bizik does not inherently teach purified complexes of α2M noncovalently associated with an antigenic molecule because the SDS-PAGE purification step used in the First Bizik Procedure would have disrupted any such complexes had they been present (see the Amendment filed August 14, 2006, pages 16 to 17). This disruption was evidenced by three references that teach that noncovalent complexes of α2M and proteins/peptides are disrupted by SDS-PAGE (see the Amendment filed August 14, 2006, pages 16 to 17). Thus, the gel-purified α2M resulting from the First Bizik Procedure did not inherently contain noncovalently complexed proteins or peptides because any noncovalent complexes of α2M and antigenic molecules that may have been present in the conditioned media used by Bizik would have been disrupted by the preparative SDS-PAGE step.

Bizik also teaches the immunoprecipitation of radiolabelled α2M from conditioned media of cancer cell lines using rabbit antiserum and fixed protein A-containing staphylococci (termed hereinafter, "the Second Bizik Procedure") (see Bizik, paragraph spanning page 82, col. 2 and page 83, col. 1; and Figure 3 on page 84). As previously discussed in the Amendment filed on August 14, 2006, the Second Bizik Procedure also does not inherently teach purified complexes of α2M noncovalently associated with an antigenic molecule because the immunoprecipitated complexes obtained comprise radiolabelled α2M, antibody, and fixed staphylococci bacteria, and as such, would not be considered purified α2M-antigenic molecule complexes (see the Amendment filed August 14, 2006, pages 17 to 18). The immunoprecipitate was subsequently subjected to SDS-PAGE but as discussed

above and previously for the First Bizik Procedure, the SDS-PAGE procedure would disrupt the noncovalent α2M-peptide/protein complexes (see Bizik at p. 85, col. 1, para. 3, and Fig. 6, the Amendment filed August 14, 2006, pages 17 to 18). It was also noted in the Amendment filed on August 14, 2006 that the α2M preparation of Bizik is not a pharmaceutical composition as recited by claim 1 because it comprises a non-pharmaceutically acceptable component, namely whole staphylococci bacteria, which, moreover, are not a pharmaceutically acceptable carrier (see the Amendment filed August 14, 2006, pages 17 to 18).

In summary, Bizik neither expressly nor inherently teaches purified complexes of α2M noncovalently associated with an antigenic molecule as specified in independent claims 1 and 7-9. Accordingly, Bizik does not anticipate claims 1, 7-9, or their dependent claims 40, 42, 50-57, and 61-64 and Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) over Bizik be withdrawn.

CONCLUSION

Applicants respectfully request entry of the amendments and remarks made herein into the file history of the present application. Withdrawal of the Examiner's rejections and an allowance of the application are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

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